REMARKS

Applicants respectively ask the Examiner to refer the responses dated March 19 and April 26, 2007. Both earlier amendments are no-compliable. The number was messed up due to computer auto-numbering. The corrected list of claims should be that "claims 2-6, 8-9, and 12-17 are canceled to simplify the prosecution process of this application and expedite it for allowance. Claims 1, 7, and 10-11 are pending." Applicants respectively ask the Examiner to restore the correct list of claims.

Claims numbering and rejection under 35 U. S. C. § 112 second paragraph

In page 6 of the Examiner's Office Action dated July 13, 2007, Claims 6 and 7 were rejected under 35 U. S. C. § 112, second paragraph as "Claim 7 recites 'The method of claim 10', and claim 10 has been cancelled. Claim 6 depends from claim 7".

On Applicants' responses dated on March 19 and April 26, 2007 to the Examiner's Office action on April 19, 2007, while Applicants respectively correct the typographical error on claim listing (the typographical error "-6" was deleted after Claim 2) , an error had been introduced into claim numbering. The correct list should be that claims 1, 7, 10, and 11 are remaining in this application and claims 2-6, 8, 9, 12-17 are canceled to expedite the prosecution process. Therefore, the list of claims is required to be corrected in this application.

After correction, it makes sense that Claim 10 is dependent on Claim 7, and Claim 11 is dependent on Claim 10.

In the following response, Claim 1, 3, 6 and 7 respectively refers to Claim 1, 7, 10 and 11 of the corrected list.

Claim Rejection Maintained

The Examiner maintains that "the amended claims 1 , 3, 6 and 7 remain rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement for reasons set forth in the previous office actions". The Examiner stated that two oligodendrocyte precursors (OLPs) cell lines (Oli-neu) and CG-4 are characterized as "undistinguishable from primary O-2A cells by morphological and immunochemical criteria".

The examiner demonstrates a lack of understanding of the historical perspective in the literature regarding lineages of myelinating cells and bases her assumptions on a single paper Crang et al. The examiner states "Crang et al. (Eur. J. Neurosci., 2004, 20(6):1445-1460) teach that myelin oligodendrocyte glycoprotein (M0G)-expressing oligodendrocyte precursors isolated from the adult rat CNS (primary culture) can differentiate into oligodendrocytes, or astrocytes and Schwann cells, depending on the culture medium components (see Abstract)". This statement this improper characterizes the referenced teachings.

1) The abstract and paper do not state or demonstrate that oligodendrocyte precursors express MOG and become astrocytes or Schwann cells. Rather, the authors say that MOG-expressing mature cells from adult spinal cord express "molecules previously considered to be restricted to oligodendrocyte progenitors". There are significant difference in these 2 statements to the artisan in this field. There is no consensus whatsoever in the literature that MOG expressing cells are undifferentiated oligodendrocytes; MOG+ cells are committed to myelinate. During development, oligodendrocyte progenitors derive from ventral spinal cord while Schwann cells derive from neural crest.

2) What this paper demonstrates is that if MOG+ cells are separated by anti-MOG coated beads, the resulting population of cells is not 100% MOG+. There is a small population of cells that is MOG-negative. A fraction (12-15%) of those cells that were MOG+ also expressed PDGFaR or A2B5, markers of cells other than oligodendrocytes including oligodendrocyte precursors, microglia, and olfactory ensheathing cells. It is clear that the isolated population of cells was not clonal and therefore could have been contaminated with either Schwann cells or cells that resemble Schwann cells. Crang et al. state on page 1457 "...it is possible that they [sic Schwann cells] could be derived from a MOG-negative precursor, which can readily be induced

to generate Schwann cells under the influence of BMPs or the acutely demyelinated environment into which the cells were transplanted".

3) The source of supposed Schwann cells which they report are derived from then MOG+ cells might also be from the area surrounding the ethidium bromide lesion the authors created. Ethidium bromide lesions kill astrocytes. Crang et al. themselves have published many papers demonstrating that in lesions where astrocytes have been eliminated, remyelination proceeds mostly by Schwann cell investment of axons. Astrocytes normally provide a glia limitans, a structure that prevents ingress of Schwann cells from the peripheral nervous system to the CNS. In their absence, Schwann cells migrate into the CNS and remyelinate.

4) The identification of some of the remyelinating cells by Crang et al. in the lesions transplanted with MOG+ cells as being Schwann cells is based on morphology and the presence of p75 and GFAP in these cells. GFAP and p75 appear on schwann cells but also on other cells capable of remyelinating the tissue. The authors state themselves (page1458): "We can not exclude the possibility that the cells generated from the anti-MOG isolation procedure could in fact be olfactory ensheathing cells (OECs) as both cell types have similar appearance when they remyelinate CNS axons and both are positive for GFAP and P75 in tissue culture."

In summary, Crang et al. admit that they have not excluded the possibility of contaminating cells introduced in the enriched but not clonal MOG+ population, the possibility of endogenous Schwann cells entering the lesion from the PNS, and most importantly, the possibility of a misidentification of OECs as Schwann cells.

This misunderstanding may lead the Examiner to the assertion that CG4 cells are is identical to primary oligodendrocytes.

Applicants do not dispute the above citation that CG-4 cell line are characterized as "undistinguishable from primary O-2A cells by morphological and immunochemical criteria". However, despite these similarities, the cells are not identical. A primary cell taken directly from a living organism is not immortalized cell line, which is defined "unique population of cells"

obtained by culture from a primary implant through numerous generations. Although they might be same in certain criteria, they are certainly different from each other in other criteria. Thus, the conclusion from the experiments using immortalized cells should not be taken as the evidence against Applicants' results and claims related to primary cells in this application.

In addition, the Office Action alleges that the specification fails to teach how to achieve "reducing exposure of oligodendrocytes and precursors to osteopontin". On page 30, line 17, Applicants clearly state that "it is desirable to minimize osteopontin production or reactivity, for example when lack of oligodendrocyte maturation is desired". The example is followed in that paragraph. On page 32, line 15, Applicants provide another method for "reducing the impact of osteopontin" to minimize expression of the receptors of osteopontin or to occupy the osteopontin receptors so that the receptors cannot engage osteopontin (lines 15-17, page 32). The practicing methods are known in the art and available to the artisan. Therefore, the allegation is improper.

New Grounds of Rejection Under 35 U.S.C § 112

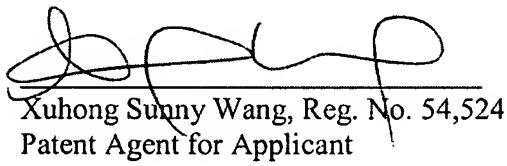
In the Office Action dated July 13, 2007, the Examiner rejected Claims 1 and 3 stating that Claims fail to comply with the enablement requirement and the claim(s) contains subject matter which was not described in the specification, specifically, the specification does not support amended claim on "primary oligodendrocytes".

On page 17 of this instant application, lines 8-9, Applicants state "osteopontin antibody can be immobilized on a solid matrix, such as a bead or a culture plate surface amd exposed to a mixed population of cells". A mixed population of cells can't be cell lines, but only primary oligodendrocytes. On page 31 of this instant application, line 15, Applicants clearly state that "osteopontin can be used therapeutically as discussed hereinabove to promote the growth and expansion of oligodendrocytes population at a particular site in the body". This is further evidence that primary oligodendrocytes are used in this invention. Applicants also state in page 39, line 5, that "because the osteopontin can find use with demylination disorders, the active agent may be preferably delivered to the central nervous system", clearly, it can't be the cell lines acted on here. In view of above statement of this instant application, primary

oligodendrocytes have been used in this invention and evidences are presented in the specification. Therefore, withdrawal of the rejection is respectively requested.

The Applicants submit that the claims, as amended, are in condition for allowance, and respectfully request early, favorable action on the application. The Commissioner is authorized to charge any fees or credit any overpayment necessitated by this response to Deposit Account No. 18-1982. Should the Examiner believe that an interview would advance the prosecution of this application, the Applicants invite him to contact the undersigned at 908.231.3648.

Respectfully submitted,



Xuhong Sunny Wang, Reg. No. 54,524
Patent Agent for Applicant

sanofi-aventis U.S. Inc.
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807
Telephone (908) 231-**3648**
Telefax (908) 231-2626

Docket No. USAV2001/0172 US NP